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Filed : March 12, 2001

REMARKS

Status of Claims

Claims 1-29, 49, and 50 remain pending in the application. The Applicants have amended Claims 1 and 21. The specific changes to the amended claims are shown above, wherein the insertions are underlined and the ~~deletions~~ are ~~stricken through~~. Applicant respectfully requests reconsideration and allowance of all claims.

Discussion of Rejection under 35 U.S.C. § 102(b)

The Examiner has rejected Claims 1-21 and 49 under 35 U.S.C. § 102(b) as allegedly anticipated by the 1995 JOURNAL OF NEUROSCIENCE METHODS article “Simultaneous Optical Recording of Evoked and Spontaneous Transients of Membrane Potential and Intracellular Calcium Concentration with High Spatio-Temporal Resolution” by Sinha et al. (“Sinha”).

In order for a reference to anticipate a claim, the reference must teach every element of the claim. “A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.” *Verdegall Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987). Applicant respectfully contends that Sinha fails to teach each of the elements in Applicant’s Claims 1 and 21.

Specifically, the Examiner claims that Sinha teaches the use of paired current pulses to stimulate cells. The Examiner further asserts, “it is an inherent property of the Tm to change in a single direction away from the starting Tm. In the hippocampal cells taught in Sinha, the [transmembrane potential] of the cells, in response to the paired pulse would *rise from* the resting [transmembrane potential] (expected to be slightly positive of the potassium equilibrium potential) to the sodium equilibrium potential (i.e.,[] a [transmembrane potential] change in a single direction), and then *back towards* the potassium equilibrium potential as the sodium channels inactivated” (emphasis added).

Claims 1 and 21 have been amended to more clearly define the differences between the transmembrane potential changes produced in the claimed invention and those induced in Sinha and the other prior art of record such as Jacobs. Specifically, these independent claims have been amended to recite “said transmembrane potential changes predominantly in a single direction

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away from a starting transmembrane potential over the course of said series of electric fields due to a continuing and additive accumulation of charge in said cell over the course of said series of electric fields." As discussed during the interview, and as shown in Figure 4B of the Sinha reference, the transmembrane potential spikes up and then back down with each pulse. There is no "continuing and additive accumulation of charge" producing a voltage change "predominantly in one direction" over the course of the pulse series. It is important to note also that the accumulation of calcium ion shown in Figure 4B of Sinha does not produce a change of membrane potential predominantly in a single direction as claimed. The transmembrane potential, illustrated in the top of Figure 4B, spikes up and down with each pulse, while the calcium concentration, shown in the middle of Figure 4B, continually rises with successive pulses.

As shown in Figure 4, 10, and 14 of the present specification, it is illustrated that the transmembrane potential predominantly changes in a single direction, away from the starting transmembrane potential, over the course of a series of pulsed electric field applications. The transmembrane potential does not spike in one direction and then return substantially to its original potential after each pulse as shown in Sinha.

Therefore, Claims 1 and 21 are allowable because Sinha fails to set forth, either expressly or inherently, every element of Claim 1 or Claim 21. For at least the reasons set forth above, Applicant respectfully requests reconsideration and allowance of Claims 1 and 21.

Discussion of Dependent Claims 2-20, 22-29, and 49

Claims 2-20, 22-29, and 49 depend from and further limit either Claim 1 or Claim 21 and are believed to be allowable at least for the reason that they depend from an allowable base claim. Applicant respectfully requests reconsideration and allowance of Claims 2-20, 22-29, and 49.

Discussion of Rejection under 35 U.S.C. § 103(a)

The Examiner has also rejected Claims 1-29 and 50 under 35 U.S.C. § 103(a) as unpatentable over WO Patent Application No. 96/41166 to Tsien et al. ("Tsien") in view of the 1997 THE JOURNAL OF NEUROSCIENCE article "Control of Action Potential-Induced Ca²⁺

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Signaling in the Soma of Hippocampal Neurons by Ca²⁺ Release from Intracellular Stores" by Jacobs et al. ("Jacobs").

The Examiner acknowledges that Tsien fails to disclose the use of electrical stimulation to modulate ion channel activity. The Examiner asserts that it would be obvious to use the electrical stimulation of Jacobs in combination with Tsien.

However, the stimulation of Jacobs is the same as that of Sinha. Jacobs does not illustrate any measurement of the transmembrane potential (Jacobs measures Ca concentration), but states in the second column of page 4130 that "[m]ost likely, each 1 msec field pulse induces a single action potential in this preparation." Thus, the neural cell cultures undergo externally induced action potentials with each stimulus. As discussed above in relation to Sinha, these action potentials do not produce a change in transmembrane potential predominantly in one direction away from a starting transmembrane potential due to a continuing and additive accumulation of charge as set forth in Claims 1 and 21. The combination of Tsien and Jacobs still fails to teach all of the claim limitations.

Discussion of Dependent Claims 2-20, 22-29, and 49-50

Claims 2-20, 22-29, and 49-50 depend from and further limit either Claim 1 or Claim 21 and are believed to be allowable at least for the reason that they depend from an allowable base claim. Applicant respectfully requests reconsideration and allowance of Claims 2-20, 22-29, and 49-50.

CONCLUSION

The Applicants have endeavored to address all of the Examiner's concerns as expressed in the outstanding Office Action. Accordingly, amendments to the claims pursuant to the Examiner's rejections under §§ 102 and 103, the reasons therefor, and arguments in support of the patentability of the pending claim set are presented above. In light of these amendments and remarks, reconsideration and withdrawal of the outstanding rejections is respectfully requested.

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Any claim amendments which are not specifically discussed in the above remarks are not made for patentability purposes, and it is respectfully submitted that the claims satisfy the statutory requirements for patentability without the entry of such amendments. These amendments have only been made to increase claim readability, to improve grammar, or to reduce the time and effort required of those in the art to clearly understand the scope of the claim language.

If the Examiner has any questions which may be answered by telephone, he is invited to call the undersigned directly. Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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